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EXAMINER
ZITOMER, STEPHANIE W

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 06/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/923,327	MURPHY, PATRICIA D.	
	Examiner	Art Unit	
	Stephanie Zitomer	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11-29-2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18,20-23,26,29,34,37-39 and 44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18,20-23,26,29,34,37-39 and 44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Application status

1. This application is a Continuation of serial no. 09/524,794, filed March 14, 2000, now abandoned, which is a Division of seril no.09/129,134, filed August 4, 1998, now abandoned.

2. Claims 18, 20-23, 26, 29, 34, 37-39 and 44 are pending.

Informalities

3. The disclosure is objected to because of the following informalities: The application is not in compliance with 37 CFR 1.821 which requires all nucleotides sequences presented in the application to have SEQ ID NOS:. The specification contains multiple tables of nucleotide sequences which do not have SEQ ID NO: identifiers.

Appropriate correction is required.

Rejection under 35 U.S.C. 112, first paragraph: Lack of written description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 22, 23, 29, 38, 39 and 44 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims are drawn to a large genus of isolated proteins or antibodies thereto or to known wild-type proteins or a large genus of isolated DNAs the respective amino acid or nucleotide sequences of which are "determinable" by claimed generic methods for determining "a new haplotype of a gene of interest or an antibody capable of binding to either a protein having a new amino acid sequence or a protein having a known wild-type amino acid sequence but not both.

The specification discloses three single nucleotide polymorphisms in non-coding intronic sequences of the MSH2 gene (page 25) and three allelic variations at two positions in the MSH1 gene (page 28) relative to given GenBank nucleotide sequences. One of the changes in the latter gene was found to change an amino acid. No antibodies are described. The description of three nucleotide changes in two genes and one amino acid change does not constitute a representative number of species of the large genera of "new haplotypes", "new wild-type amino acid sequences" and "new polymorphisms" encompassed by the claims. The specification thus provides insufficient written description to support the genus encompassed by the claims in each instance. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed."* (See page 1117) In the instant case, the specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.) With the exception of the cited alterations in the MSH1 and MSH2 genes and amino acid sequence, the skilled artisan cannot envision the detailed chemical structure of the encompassed DNAs and/or proteins, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993), and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence. Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

> To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In *re Gosteli*, 872 F.2d 1008, 1012, 10

> USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.
>
> An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. *Fiers v. Revel*, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.

Accordingly, the specification does not provide a written description of the invention of claims 22, 23, 29, 38, 39 and 44.

Rejections under 35 U.S.C. 112, second paragraph: Indefiniteness

> The following is a quotation of the second paragraph of 35 U.S.C. 112:
>
> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 18, 20-23, 26, 29, 34, 37-39 and 44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(a) The term "wild-type" is a relative term as is clear from the discussion at page 2, the last paragraph, and page 3, wherein the designation of a gene as "wild-type" appears to depend on the particular gene, whether it is representative of the population at large and whether it is a plant gene or an animal gene or from some other type of organism. Thus, neither the claims nor the specification set out the necessary criteria for defining or identifying a "wild-type" gene. Absent any definition in the specification or claims it is suggested to replace "wild-type" with a meaningful term or description.

(b) The word "each", as used in the claims, is ungrammatical and lacks antecedent basis. For example, in claim 18, "each" which has as its antecedent, "one" in "at least

one", is inappropriate because "each" means "one of many". It is suggested to change "each" in "each" occurrence to --at least one-- which corresponds with the antecedent. This correction pertains to claims 18, 26 and 34.

(c) The claims are confusing due to the ungrammatical use of "where". It is suggested to change "where" to --wherein--. "Where" refers to location whereas "wherein" means "in what way', i.e., in claim construction, it means a further explanation or refinement of the preceding recitation.

Rejections under 35 U.S.C. 102(e): Anticipation

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

6. Claims 18, 20-23, 26, 29 and 44 are rejected under 35 U.S.C. 102(e) as being anticipated by the patent to Pesonen et al. (5,763183). Regarding claim 18, the claimed invention method for determining a new haplotype of a gene of interest wherein at least one "wild-type" nucleotide sequence of the gene of interest is known is disclosed by Pesonen et al.: the "known nucleotide sequence" is that of the gene of interest, the gene encoding the "wild-type" 5-HT_7 receptor (column 2, lines 39-48; 62-64). The claimed method is disclosed as follows: comprising (a) selecting at least one individual having a genetic history indicating inheritance of functional alleles of the gene of interest (column 5, lines 24-35); (b) determining the nucleotide sequence of the gene or a fragment thereof in at least one allele of the individual (column 5, line 66-column 6, line 1); (c) comparing each nucleotide sequence from the individual to that of each "wild-type" nucleotide sequence,

wherein the presence of at least one nucleotide sequence different from each known "wild-type" nucleotide sequence indicates the presence of a new haplotype (column 6, lines 24-26) and if the new haplotype is not determined by step (c), repeating steps (a), (b) and (c) with a different individual until the new haplotype is determined (column 6, lines 59-61).

Regarding claim 20, Pesonen et al. discloses the embodiment wherein the individual is a human (column 2, lines 49-55).

Regarding claim 21, Pesonen et al. discloses the embodiment wherein the new haplotype encodes a protein having at least one amino acid difference in its deduced amino acid sequence from a protein encoded by at least one "wild-type" nucleotide sequence (e.g., column 2, lines 43-46.

Regarding claim 22, Pesonen et al. discloses the embodiment comprising an isolated protein encoded by the new haplotype determinable by the method of claim 21 (column 3, lines 4-8).

Regarding claim 23, Pesonen et al. discloses the embodiment comprising an isolated DNA comprising the nucleotide sequence of the new haplotype of the gene of interest determinable by the method of claim 18 (column 2, line 64-column 3, line 3).

Regarding claim 26, Pesonen et al. discloses the claimed method for determining a new "wild-type" amino acid sequence of a protein of interest wherein at least one "wild-type" amino acid sequence of the protein is known comprising the steps of: (a) selecting at least one individual having a genetic history indicating inheritance of functional alleles of a gene encoding the protein of interest (column 6, lines 49-58); (b) determining or deducing at least on amino acid sequence of the protein produced by the individual; (c) comparing each of said amino aci sequences from the individual to that of each "wild-type" amino acid sequence, wherein the presence of at least one amino acid difference from each known "wild-type" amino acid sequence indicates the presence of a new "wild-type amino acid sequence (column 7, lines 12-19) and if the new "wild-type" amino acid sequence is not determined by step (c), repeating steps (a), (b) and (c) with a different

individual until the new "wild-type" amino acid sequence for the protein of interest is determined (column 6, lines 49-58).

Regarding claim 29, Pesonen et al. discloses the embodiment comprising a protein having the new amino acid sequence of the protein of interest determinable by the method of claim 26 (column 3, lines 4-8).

Regarding claim 44, Pesonen et al. discloses the embodiment comprising an antibody capable of binding to the isolated protein having a new amino acid sequence (column 3, lines 27-32; columns 8-10, Examples 3 and 4).

7. Claims 34 and 39 are rejected under 35 U.S.C. 102(e) as being anticipated by the patent to Santamaria et al. (5,578,443). The claimed invention method for determining a new polymorphism of a gene of interest wherein at least one "wild-type" nucleotide sequence of the gene of interest is known is disclosed by Santamaria et al.: the known "wild type" nucleotide sequence" is that of the gene of interest, the genes encoding the "wild-type" Class II HLA genes (column , lines 32-45). Regarding claim 34, the claimed method is disclosed as follows: comprising (a) selecting at least one individual having a genetic history indicating inheritance of functional alleles of the gene of interest (column 28, lines 1-3); (b) determining a nucleotide sequence of the gene or a fragment thereof in at least one allele of the individual (column 28, lines 17-48); (c) comparing each nucleotide sequence from the individual to that of each "wild-type" nucleotide sequence, wherein the presence of at least one nucleotide sequence different from each known "wild-type" nucleotide sequence indicates the presence of a new polymorphism (column 28, lines 56-58; column 8, lines 42-45) and if the new polymorphism is not determined by step (c), repeating steps (a), (b) and (c) with a different individual until the new polymorphism is determined (column 19, lines 35-39). Regarding claim 39, Santamaria et al. discloses the embodiment comprising an isolated DNA comprising the nucleotide sequence of the gene having the new polymorphism determinable by the method of claim 34 (column 28, lines 33 and 48).

Rejection under 35 U.S.C. 103(a): Obviousness

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 37 and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Santamaria et al. as applied to claim 34 and 37 above and further in view of additonal teachings in the patent. Regarding claim 37, the embodiment comprising the method of claim 34 wherein the gene having the new polymorphism encodes a protein having at least one amino acid difference in its deduced amino acid sequence from a protein encoded by the at least one "wild-type" nucleotide sequence, it would have been obvious at the time the claimed invention was made to deduce the amino acid sequence for the obvious benefit of determining whether the polymorphism caused a change in the protein which might affect the phenotype of the individual (column 4, lines 61-65) and identifying the region of the HLA antigen in which the polymorphism was located (column 2, lines 10-15). Regarding claim 38, the embodiment comprising the isolated protein encoded by the gene having a new polymorphism determinable by the method of claim 37, the skilled practitioner in the art would have been motivated further to obtain the isolated protein for the obvious benefit of its utility in improving standard serological testing with additional new polymorphisms (column 2, lins 56-61).

Conclusion

9. **No claim is allowed.**

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephanie Zitomer whose telephone number is (703) 308-3985. The examiner can normally be reached on Monday through Friday from 9:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152. The official fax phone number for this Group is (703) 308-4242. The unofficial fax number is (703) 308-8724. The examiner's Rightfax number is 703-746-3148.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196. For questions and requests relating to formal matters contact LIE Chantae Dessau at 703-605-1237.

S. Zitomer

Stephanie Zitomer, Ph.D.

June 16, 2003

STEPHANIE W. ZITOMER
PRIMARY EXAMINER